

CAGCGTCAGACGCAGGGCACTGAGAATGTGCGACAGCGCGCAACGATGAAGTAGCCCAGAGGGTCCCTTG  
 GAAAATGAGGCCAGGGTCCCTGCTGCTGCTTGTCTGCTGCTCGCCCTGTCCAGGAGCCTGCGGGGCAAA  
 GAGTGTGCGTCTCCACCCTGTGAGTGTACCAGGAGGACGACTTCAGAGTCACCTGCAAGGAGCTCCACC  
 GAATCCCCAGCCTGCCGCCAGCACCCAGACTCTGAAGCTCATCGAGACTCATCTGAAGACCATACCCAG  
 TCTTGCAATTTTCGAGTCTGCCCAATATTTCCAGGATCTATTTATCTATAGATGCAACTCTGCAGCGGCTG  
 GAACCACATTCTTTCTACAATTTGAGTAAAATGACTCACATAGAAATCCGGAACACCAGAAGCTTAACCT  
 ATATAGACCCTGATGCCCTTGACAGAGCTCCCCTTGCTCAAGTTTCTTGGCATTTCATACTGGACTTAG  
 AATATTCCTGACTTGACCAAAATTTATTCCACGGACATATTCTTTATACTTGAAATCACAGACAACCCT  
 TACATGACTTCGGTCCCTGAAAACGCATTCCAGGGCCTATGCAATGAAACCTTGACCCTGAAACTGTACA  
 ACAATGGATTTACTTCAGTCCAAGGACATGCTTTCAATGGAACAAAGCTGGATGCTGTTTACCTAAACAA  
 GAATAAATACCTGACAGCTATAGACAACGATGCCTTTGGAGGAGTATACAGTGGACCAACTTTGCTAGAT  
 GTGTCTTCCACCAGCGTCACTGCCCTTCCTTCCAAAGGCCTGGAGCACCTCAAAGAACTGATCGCAAAAG  
 ACACCTGGACTCTCAAAAAGCTCCCGCTGTGCTTGAGTTTCCTCCACCTCACTCGGGCTGACCTCTCTTA  
 CCCGAGCCACTGCTGCGCTTTTAAGAACCAGAAGAAAATCAGGGGAATCCTGGAGTCTTTGATGTGTAAT  
 GAGAGCAGTATCCGGAACCTTCGTCAAAGGAAATCAGTGAACATCTTGAGGGGTCCCATCTACCAGGAAT  
 ATGAAGAAGATCCGGGTGACAACAGTGTGGGTACAAACAAAACCTCCAAGTTCAGGAGAGCCCCAAGCAA  
 CTCTCACTATTACGTCTTCTTGAAGAACAAGAGGATGAGGTCGTTGGTTTCGGCCAAGAGCTCAAAAAT  
 CCTCAGGAAGAGACTCTCCAAGCCTTCGAGAGCCACTATGACTACACGGTGTGTGGGGACAACGAGGACA  
 TGGTGTGTACCCCCAAGTCCGACGAGTTTAACCCCTGTGAAGATATCATGGGCTACAGGTTCTGAGAAT  
 CGTGGTGTGGTTTGTGCTGCTGCTGCTCCTGGGCAATATCTTCGTCCTGCTCATTCTGCTAACCAGC  
 CACTACAAATTGACCGTGCCGCGTTTCTCATGTGCAACTTGGCCTTTGCAGATTTCTGCATGGGGGTAT  
 ACCTGCTTCTCATTGCCCTCTGTAGACCTGTACACACACTCTGAGTACTACAACCACGCCATCGACTGGCA  
 GACGGGCCCTGGGTGCAACACGGCTGGCTTCTTCACTGTTTTCGCCAGTGAGTTATCAGTGTACACACTG  
 ACGGTCACTACCCCTGGAGCGATGGTACGCCATCACCTTCGCCATGCGCCTGGATAGGAAGATCCGCCTCA  
 GGCACGCGTACACCATCATGGCTGGGGGCTGGGTTTCTGCTTCTTCTCGCCCTGCTCCCGATGGTGGG  
 AATCAGCAGCTATGCCAAGGTCAGCATCTGCCTGCCAATGGACACCGACACCCCTCTTGCACTCGCATAC  
 ATTGTCCTCGTTCTGCTGCTCAATGTTGTTGCCTTTGTTGTCGTCTGTTCTGCTATGTGAAGATCTACA  
 TCACGGTCCGAAATCCCCAGTACAACCCCTCGAGATAAAGACACCAAGATTGCCAAGAGGATGGCTGTGTT  
 GATCTTCACTGACTTCATGTGCATGGCGCCCATCTCCTTCTATGCGCTGTGCGCACTTATGAACAAGCCT  
 CTAATCACTGTTACTAACTCCAAAATCTTGTTGGTTCTTCTTACCCCTCAACTCCTGTGCCAATCCGT  
 TTCTCTATGCTATTTTCACCAAGGCCTTCCAGAGGGACGTGTTTCATCCTGCTCAGCAAGTTTGGCATCTG  
 CAAACGCCAGGCCAGGCCTATCAGGGTCAGAGAGTCTGTCCCAACAATAGCACTGGTATTGAGATCCAA  
 AAGATTTCCCGAGGACACGAGGACAGTCTCCCCAACATGCAAGATACCTATGAACTGCTTGGAAACTCCC  
 AGCTAGCTCCAAAACGTCAGGGACAAATCTCAGAAGAGTATAAGCAAACAGCCTTGTAAGGAAAGGCTA  
 CGCTAGTCACAGTGAGACTTACAAAAGGCTGGTTTTCTTGAACATGCGTTCCAGTCCCGTGACATGTGAAC  
 ACATAGGTTTCATGCAGGTGATGATTCATAGGGTCAGAGTTCATCTCTAGAAAGTATTGCCTC (SEQ ID NO:1)

FIGURE 1A

MRPGSLLLLVLLLALSRLRGKECASPPCECHQEDDFRVTCKELHRIPSLPPSTQTLKLIETHLKTIPSLAFSSLPN  
ISRIYLSIDATLQRLPHSFYNLSKMTHEIRNTRSLTYIDPDALTELPLLKFLGIFNTGLRIFPDLTKIYSTDIFF  
ILEITDNPYMTSVPENAFQGLCNETLTLKLYNNGFTSVQGHAFNGTKLDAVYLNKNKYLTALDNDAFGGVYSGPTLL  
DVSSTSVTALPSKGLEHLKELIAKDTWTLKKLPLSLSFLHLTRADLSYPHCCAFKNQKKIRGILESLMCNESSIRN  
LRQRKSVNLRGPIYQEYEEDPGDNSVGKQNSKFQESPSNSHYVFFEEQEDEVVGFGQELKNPQEETLQAFESHY  
DYTVCGDNEDMVCTPKSDEFNPCEDIMGYRFLRIVVWFVSLALLGNIFVLLILLTSHYKLTVPFLMCNLAFADFC  
MGVYLLLIASVDLYTHSEYYNHAIWQTGPGCNTAGFFTTFASELSVYTLTVITLERWYAITFAMRLDRKIRLRHAY  
TIMAGGWVSCFLLALLPMVGISSYAKVSI CLPMDTDTPLALAYIVLVLNVAFFVVVCSYVKIYITVRNPQYNPR  
DKDTKIAKMAVLIFTDFMCMAPISFYALSALMNKPLITVTNSKILLVLFYPLNSCANPFLYAIFTKAFQRDVFILL  
SKFGICKRQAQAYQGQRVCPNNSTGIQIQIPQDTRQSLPNMQDTYELLGNSQLAPKLQGQISEEYKQTAL (SEQ  
ID NO:2)

FIGURE 1B

T004644-10001

underlined = deleted in targeting construct

[ ] = sequence flanking Neo insert in targeting construct

[CAGCGTCAGACGCAGGGCACTGAGAATGTGCGACAGCGCGCAACGATGAAGTAGCCAG  
 AGGGTCCCTTGGAAAATGAGGCCAGGGTCCC] TGCTGCTGCTTGTTCTGCTGCTCGCCCT  
GTCCAGGAGCCTGCGGGGCAAAGAGTGTGCGTCTCCACCCTGTGA [GTGTCACCAGGAGG  
 ACGACTTCAGAGTCACCTGCAAGGAGCTCCACCGAATCCCCAGCCTGCCGCCAGCACCC  
 AGACTCT] GAAGCTCATCGAGACTCATCTGAAGACCATACCCAGTCTTGCAATTTTCGAGT  
 CTGCCCCAATATTTCCAGGATCTATTTATCTATAGATGCAACTCTGCAGCGGCTGGAACCA  
 CATTCTTTCTACAATTTGAGTAAAATGACTCACATAGAAATCCGGAACACCAGAAGCTTA  
 ACCTATATAGACCCTGATGCCTTGACAGAGCTCCCTTGCTCAAGTTTCTTGGCATTTC  
 AATACTGGACTTAGAATATTCCCTGACTTGACCAAAATTTATTCCACGGACATATTCTTT  
 ATACTTGAAATCACAGACAACCTTACATGACTTCGGTCCCTGAAAACGCATTCCAGGGC  
 CTATGCAATGAAACCTTGACCCTGAACTGTACAACAATGGATTTACTTCAGTCCAAGGA  
 CATGCTTTCAATGGAACAAAGCTGGATGCTGTTTACCTAAACAAGAATAAATACCTGACA  
 GCTATAGACAACGATGCCTTTGGAGGAGTATACAGTGGACCAACTTTGCTAGATGTGTCT  
 TCCACCAGCGTCACTGCCCTTCCCTCCAAAGGCCTGGAGCACCTCAAAGAACTGATCGCA  
 AAAGACACCTGGACTCTCAAAAAGCTCCCGCTGTCGTTGAGTTTCTCCACCTCACTCGG  
 GCTGACCTCTCTTACCCGAGCCACTGCTGCGCTTTAAGAACCAGAAGAAAATCAGGGGA  
 ATCCTGGAGTCTTTGATGTGTAATGAGAGCAGTATCCGGAACCTTCGTCAAAGGAAATCA  
 GTGAACATCTTGAGGGGTCCCATCTACCAGGAATATGAAGAAGATCCGGGTGACACAGT  
 GTTGGGTACAAAACAAACTCCAAGTTCCAGGAGAGCCCAAGCAACTCTCACTATTACGTC  
 TTCTTTGAAGAACAAGAGGATGAGGTCGTTGGTTTCGGCCAAGAGCTCAAAAATCCTCAG  
 GAAGAGACTCTCCAAGCCTTCGAGAGCCACTATGACTACACGGTGTGTGGGGACAACGAG  
 GACATGGTGTGTACCCCCAAGTCGGACGAGTTTAACCCCTGTGAAGATATCATGGGCTAC  
 AGGTTCCCTGAGAATCGTGGTGTGGTTTGTCACTCTGCTGGCTCTCTGGGCAATATCTTC  
 GTCCTGCTCATTCTGCTAACCAGCCACTACAAATTGACCGTGCCGCGGTTCCCTCATGTGC  
 AACTTGGCCTTTGAGATTTCTGCTGAGGGGTATACCTGCTTCTCATTGCCTCTGTAGAC  
 CTGTACACACACTCTGAGTACTACAACCACGCCATCGACTGGCAGACGGGCCCTGGGTGC  
 AACACGGCTGGCTTCTTCACTGTTTTCGCCAGTGAGTTATCAGTGTACACACTGACGGTC  
 ATCACCTGGAGCGATGGTACGCCATCACCTTCGCCATGCGCCTGGATAGGAAGATCCGC  
 CTCAGGCACGCGTACACCATCATGGCTGGGGGCTGGGTTTCTGCTTCTTCTCGCCCTG  
 CTCCCGATGGTGGGAATCAGCAGCTATGCCAAGGTCAGCATCTGCCTGCCAATGGACACC  
 GACACCCCTCTTGCACTCGCATACATTGTCCTCGTTCTGCTGCTCAATGTTGTTGCCTTT  
 GTTGTCTGCTGTTTCTGCTATGTGAAGATCTACATCACGGTCCGAAATCCCCAGTACAAC  
 CCTCGAGATAAAGACACCAAGATTGCCAAGAGGATGGCTGTGTTGATCTTCACTGACTTC  
 ATGTGCATGGCGCCCATCTCCTTCTATGCGCTGTGCGCACTTATGAACAAGCCTCTAATC  
 ACTGTTACTAACTCCAAAATCTTGTGGTTCTCTTCTACCCCTCAACTCCTGTGCCAAT  
 CCGTTTCTCTATGCTATTTTACCAGGCCCTCCAGAGGGACGTGTTTCATCCTGCTCAGC  
 AAGTTTGGCATCTGCAAACGCCAGGCCAGGCCATCAGGGTCAGAGAGTCTGTCCCAAC  
 AATAGCACTGGTATTTCAGATCCAAAAGATTCCCAGGACACGAGGCAGAGTCTCCCAAC  
 ATGCAAGATACCTATGAACTGCTTGAAACTCCAGCTAGCTCCAAAACCTGCAGGGACAA  
 ATCTCAGAAGAGTATAAGCAAACAGCCTTGTAAAGGAAAGGCTACGCTAGTCACAGTGAG  
 ACTTACAAAAGGCTGGTTTCTTGAACATGCGTTCCAGTCCCGTGACATGTGAACACATAG  
 GTTCATGCAGGTGATGATTATAGGGTCAGAGTTCATCTCTAGAAAGTATTGCCTC

**FIGURE 2A**

## Gene Sequence Structure

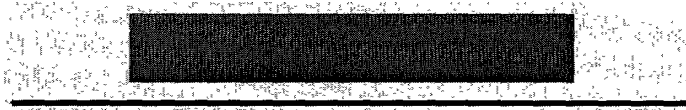
\*

91 bp

Sequence Deleted

163 bp

Size of full-length  
cDNA: 2512 bp

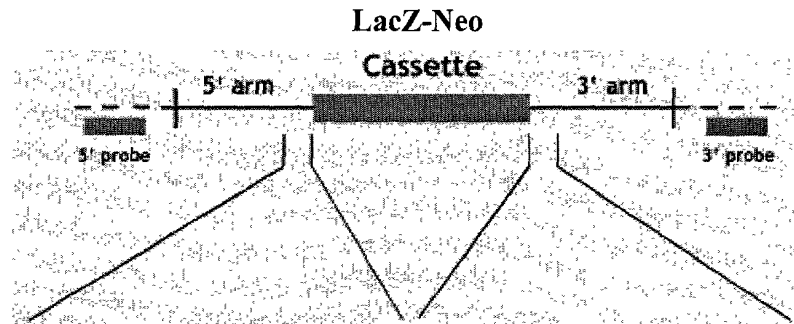


## Targeting Vector\* (genomic sequence)

Arm Length:

5': 5 kb

3': 1.3 kb



5' >ACTTGAGAGCCTCTCCTTCCC  
CCTCTCCAGCGTGCTCTCCAGCGA  
TGAGGTCACAGCCCCTCGGAGCCC  
TCCTCCTCCCTCCCTTCCCCCTCCT  
GCACCCGGGTCTCTTCCAGCGTCA  
GACGCAGGGCACTGAGAATGTGGC  
GACAGCGCGCAACGATGAAGTAGC  
CCAGAGGGTCCCCTTGGAAAATGAG  
GCCAGGGTCCC<3'  
(SEQ ID NO:3)

5' >GTGTCACCAGGAGGACGACTT  
CAGAGTCACCTGCAAGGAGCTCCA  
CCGAATCCCCAGCCTGCCGCCAG  
CACCCAGACTCTGTGAGTAGCCAA  
GGCCAAGACCCCCCCCCCCCCGAGA  
AATTCGTGGTGTGTGTGGGGTGT  
GCGCGGATATCTGGTCAGTCCCTG  
TACAAATTCAATCCCCCATGCTCG  
GGAAGGTCAGC<3'  
(SEQ ID NO:4)

Targeting Vector

Endogenous Locus

\* Not drawn to scale

FIGURE 2B

	Gender	Age (days)	Length (cm)	Body		Spleen/		Liver/		Kidney/		Thymus/		Heart/		Testes + Epididymis	
				Weight (g)	Weight (%)	Weight (g)	Weight (%)	Weight (g)	Weight (%)	Weight (g)	Weight (%)	Weight (g)	Weight (%)	Weight (g)	Weight (%)	Weight (g)	Weight (g)
+/-	Female	48	10	22.339	0.095	0.425	1.256	5.622	0.327	1.464	0.082	0.367	0.155	0.694			
+/-	Female	48	8.25	16.960	0.052	0.307	0.900	5.307	0.220	1.297	0.060	0.354	0.122	0.719			
+/-	Male	48	9.5	24.550	0.069	0.281	1.388	5.654	0.342	1.393	0.055	0.224	0.119	0.485		0.224	
+/-	Male	48	9.7	23.792	0.081	0.340	1.192	5.010	0.304	1.278	0.063	0.265	0.133	0.559		0.226	
-/-	Female	48	8.5	22.619	0.080	0.354	1.272	5.624	0.238	1.052	0.080	0.354	0.121	0.535			
-/-	Male	48	9	24.040	0.072	0.300	1.344	5.591	0.322	1.339	0.062	0.258	0.137	0.570		0.181	
-/-	Female	47	7.5	9.026	0.008	0.089	0.435	4.819	0.110	1.219	0.010	0.111	0.045	0.499			
-/-	Female	48	7	8.360	0.016	0.191	0.382	4.569	0.110	1.316	0.004	0.048	0.051	0.610			
-/-	Female	48	8	11.640	0.016	0.137	0.586	5.034	0.127	1.091	0.031	0.266	0.053	0.455		0.087	
-/-	Male	48	7.6	11.733	0.018	0.153	0.666	5.676	0.134	1.142	0.034	0.290	0.053	0.452		0.180	
-/-	Male	48	8	12.545	0.024	0.191	0.778	6.202	0.146	1.164	0.035	0.279	0.060	0.478		0.076	
-/-	Male	48	7	8.070	0.007	0.087	0.366	4.535	0.095	1.177	0.001	0.012	0.042	0.520			

FIGURE 3

Gender	Age at Test (days)	Length (cm)	Body		Spleen/		Liver/		Kidney/		Thymus/		Heart/		Testes + Epididymis Weight (g)
			Weight (g)	Weight (g)	Weight (g)	Weight (%)	Weight (g)	Weight (%)	Weight (g)	Weight (%)	Weight (g)	Weight (%)	Weight (g)	Weight (%)	
+/- Female	308	9.5	25.191	0.222	0.8813	0.8813	1.476	5.8592	0.353	1.4013	0.039	0.1548	0.145	0.5756	0.35 0.387
+/- Female	308	9.918	28.180	0.091	0.3229	0.3229	1.447	5.1348	0.383	1.3591	0.043	0.1526	0.136	0.4826	
+/- Male	308	11.025	55.089	0.182	0.3304	0.3304	3.267	5.9304	0.694	1.2598	0.074	0.1343	0.219	0.3975	
+/- Male	308	11	42.613	0.136	0.3192	0.3192	2.144	5.0313	0.485	1.1382	0.052	0.1220	0.201	0.4717	0.401 0.389
-/- Female	307	7.978	19.561	0.030	0.1534	0.1534	0.863	4.4118	0.184	0.9406	0.040	0.2045	0.109	0.5572	
-/- Male	307	9.47	25.557	0.077	0.3013	0.3013	1.394	5.4545	0.340	1.3304	0.025	0.0978	0.111	0.4343	
-/- Male	307	9.5	25.263	0.051	0.2019	0.2019	1.232	4.8767	0.296	1.1717	0.027	0.1069	0.102	0.4038	0.389

FIGURE 4